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[Qualitative Protocol]

Factors that influence parents' and informal caregivers' acceptance of routine childhood vaccination: a qualitative evidence synthesis

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ABSTRACT

This is a protocol for a Cochrane Review (Qualitative). The objectives are as follows:

1. Identify, appraise and synthesise qualitative studies exploring: parents' and informal caregivers' views, experiences, or decision-making regarding routine childhood vaccination; or the factors influencing acceptance of routine childhood vaccination arising from parents' and informal caregivers' accounts.

2. Develop a conceptual understanding of what and how different factors influence parental acceptance of routine childhood vaccination.

3. Explore how the findings of this review can enhance our understanding of the related intervention reviews (Saeterdal 2014; Oyo-Ita 2016; Jacobson 2018; Kaufman 2018).

BACKGROUND

Vaccination is considered one of the most effective public health interventions for reducing infant and child morbidity and mortality globally (CDC 1999; WHO 2018a). Vaccination programmes have led to the global eradication of smallpox, and large reductions in disability and death from polio, measles, tetanus, rubella, and diphtheria (CDC 1999; Andre 2008). To be successful, vaccination programmes depend on high levels of vaccination uptake. Not only does this provide direct protection for vaccinated individuals, it also induces indirect protection for the overall commu-

nity ("herd immunity") by slowing transmission of disease (Fine 2011). This in turn decreases the risk of infection among those who remain susceptible in the community and helps prevent disease outbreaks.

In 2016, over 19 million children did not receive the full series of basic vaccinations globally, which resulted in numerous vaccine-preventable disease outbreaks and child deaths (Feldstein 2017). While low- and middle-income countries (LMICs) bear the largest proportion of under-vaccinated or non-vaccinated children (Feldstein 2017), high-income countries (HICs) are also affected by sub-optimal vaccination. National coverage rates in many HICs remain below aspirational targets and have shown only modest progress toward meeting those targets, despite concerted efforts to improve vaccination uptake (Corben 2016; de Figueiredo 2016). National vaccination estimates also mask subnational and subgroup variations, and the low vaccination coverage rates in certain populations in HICs (Omer 2009; Scheifele 2014; Hill 2015; Hull 2017).

Supply factors, such as inadequate availability of vaccines, poor service access, or low prioritisation of vaccines for public health spending, remain important contributors to sub-optimal childhood vaccination coverage (WHO 2013a; WHO 2018a). A number of studies in both HICs and LMICs have found access barriers to be a significant reason for children not being up-to-date with their vaccinations (Rainey 2011; Machingaidze 2013a; Pearce 2015; Nadeau 2016). Studies have also found that system-level interventions - such as integrating vaccination with other services (Oyo-Ita 2016), or reducing missed opportunities for vaccination (Jaca 2018) - are effective in improving childhood vaccination coverage.

However, ensuring that parents decide to make use of available vaccines and vaccination services in a timely and appropriate manner is an additional challenge (Hickler 2015; Suk 2015). A range of studies and some reviews have revealed that a growing number of parents are questioning vaccines, seeking alternative vaccination schedules, and deciding to delay or refuse vaccination for their children, both in high- and low-income settings (Larson 2014; Dube 2015; Corben 2016). While there is increasing attention being paid to the demand-side of vaccination, we currently lack a comprehensive understanding of what, and how, different factors influence childhood vaccination acceptance (Corben 2016; WHO 2018a). Qualitative research can contribute to this understanding and help inform policy and practice, including the development of more relevant, acceptable and effective interventions to promote public acceptance and uptake of childhood vaccination.

Description of the topic

The specific research question we aim to address in the synthesis is: What, and how do, different factors influence parental acceptance of routine childhood vaccination? There is growing recognition that traditional understandings of individuals and groups as either 'anti-' or 'pro-' vaccines are inadequate; rather, attitudes and behaviours regarding vaccine acceptance are thought to exist along a continuum, from rejection of all vaccines to active support of all immunisation recommendations (Feemster 2013; Larson 2014; NVCA 2015). Vaccine hesitancy is seen to fall in the middle of this continuum. The World Health Organization (WHO) defines vaccine-hesitant individuals as: "a heterogeneous group who hold varying degrees of indecision about specific vaccines or vaccination in general. Vaccine hesitant individuals may accept all vaccines but remain concerned about vaccines, some may refuse or delay some vaccines, but accept others; some individuals may refuse all vaccines" (WHO 2014).

It is also increasingly recognised that vaccine acceptance attitudes and behaviours are complex, and are influenced by multiple factors that vary depending on time, place, and vaccines (Dube 2013; Larson 2014; MacDonald 2015; Corben 2016). A number of contrasting theoretical frameworks have been proposed in an attempt to understand these influencing factors. The WHO developed a 'Three C' framework, including axes of confidence (trust in effectiveness and safety of vaccines and the systems that deliver them), complacency (low perceived risk of vaccine-preventable diseases), and convenience (affordability and access) (WHO 2013b; MacDonald 2015). Betsch and colleagues added two additional items to this framework (calculating and collective responsibility), to encompass cost-benefit reasoning and concerns for the protection of others, both of which have a role in some parents' vaccination decisions (Betsch 2015; Betsch 2018). The 'C frameworks' seek to identify the psychological determinants of vaccine acceptance and hesitancy, drawing on psychological models of decision-making behaviour, such as the health belief model (HBM) and the theory of planned behaviour (TPB). In contrast, Peretti-Watel and colleagues have reformulated the 'C frameworks' to incorporate the major structural features of contemporary societies (Peretti-Watel 2015). Their model conceptualises vaccine hesitancy and acceptance as a two-dimensional decision-making process, that depends on people's level of commitment to modern society's risk culture, or "healthism", and their trust in the authority of healthcare providers and mainstream medicine.

Alternative approaches have drawn on adaptations of ecological models of health behaviour to identify the multiple and interrelated levels of influence impacting on vaccine acceptance, hesitancy, and refusal (Sturm 2005; Callreus 2010; WHO 2013b; Larson 2014). For example, the WHO has developed a 'Vaccine Hesitancy Determinants Matrix', which categorises factors under three domains: contextual influences, including sociocultural and health systems factors; individual and group influences, including those arising from personal perceptions of a vaccine; and vaccine- or vaccination-specific issues, including individual assessments of risks and benefits and the effects of the mode of administration (WHO 2013b; MacDonald 2015).

There is, therefore, no agreed framework for understanding the factors influencing vaccine acceptance. In addition, while current models have provided important insights into what factors potentially influence vaccine acceptance, few provide a comprehensive and holistic understanding of how these factors operate and interact (Cooper 2019). In addition, few of the existing models are based on empirical qualitative evidence. For example, the WHO's 'Three C' framework was developed by reviewing existing conceptual models for grouping vaccine hesitancy determinants, and by taking into consideration model complexity, understandability, global applicability, breadth of factors considered, and potential usefulness in informing the development of vaccine hesitancy indicators and survey questions (MacDonald 2015). Similarly, the WHO's 'Vaccine Hesitancy Determinants Matrix' was derived from determinants identified in a commissioned systematic (quantitative) review of determinants, the collective experience and insights of members of the WHO's Strategic Advisory Group of Experts on Immunization (SAGE) working group on vaccine hesitancy, and consultation with experts working in the field (Larson 2014; MacDonald 2015). The commissioned systematic review of determinants concluded that "Future consideration of qualitative studies in all regions would help…enhance understanding around decision-making processes and the ways in which explanatory factors come together to influence vaccination behavior" (Larson 2014).

This review will synthesise qualitative evidence on parents' and informal caregivers' views, experiences or decision-making regarding routine childhood vaccination, in an attempt to identify the most relevant factors influencing vaccination acceptance and to build and refine theory about how these factors come together to influence vaccination acceptance. This might contribute to the development or refinement of conceptual models on vaccination acceptance which are built on a broader evidence-base and which are more theoretical in nature. In this review we will focus specifically on studies that report on the views of parents and informal caregivers, and not those of other relevant stakeholders. This is because our intention is to understand the factors considered important by, and meaningful to, vaccine target users themselves in contributing to vaccination acceptance. If they report that others have an influence on their acceptance of vaccination, this will be captured by the review findings.

Why is it important to do this synthesis?

Currently, there is a large global focus on the demand-side of vaccination. Various international working groups have been established to investigate this topic: a working group on vaccine hesitancy within the WHO's SAGE was formed in 2012 (Schuster 2015); a working group on vaccine confidence was established in the National Vaccine Advisory Committee (NVAC) in the USA in 2013 (NVCA 2015); and an informal working group on vaccine demand was initiated in 2015, under the leadership of the United Nations International Children's Emergency Fund (UNICEF) and in collaboration with the WHO (Hickler 2017). In addition, in 2018 the WHO's SAGE indicated that "Demand-related issues like vaccine hesitancy are complex, and subject to multiple influences. The need is pressing to better understand the drivers of and barriers to vaccination uptake and to build national capacities to develop and implement tailored strategies to promote demand for immunization services" (WHO 2018a). A year later, in 2019,the WHO also identified vaccine hesitancy as one of the ten main threats to global health in 2019 (WHO 2019). This increased focus on vaccine acceptance is the consequence of a number of factors, including settings with low or stagnated rates of vaccination (de Figueiredo 2016; Hull 2017); recent global outbreaks of largely eliminated vaccine-preventable diseases, such as measles, which have been linked to under-vaccination (Dabbagh 2018; Larson 2018a); concerns about the rise of vaccine hesitancy (Hickler 2015; Lane 2018); more vaccines becoming available; and more diseases becoming the focus of eradication campaigns (WHO 2013a).

To support decision making within vaccination programmes regarding effective strategies to increase and sustain public uptake of childhood vaccination, it is important to understand which factors promote and inhibit acceptance of vaccination. In particular, understanding parents' and informal caregivers' reasons for accepting or declining vaccination could help inform the development of interventions to improve uptake of vaccines that are better aligned with the norms, views, expectations and potential concerns of target users, thereby potentially enhancing their acceptability and effectiveness. As stressed by Larson and colleagues "emphasis should be placed on listening to the concerns and understanding the perceptions of the public to inform risk communication and to incorporate public perspectives in planning vaccine policies and programmes" (Larson 2011).

Qualitative research is well-placed for exploring complex beliefs, behaviours, and decision-making, and for understanding how different factors influence these. Data arising from qualitative studies can help answer questions regarding what people think about vaccines, how they experience vaccination, their vaccination decision-making processes, and the reasons for these views, experiences and decisions. A better understanding of these issues, and their impact in different settings, can help identify what and how different factors influence childhood vaccination acceptance. This in turn can help us think through which interventions may be most appropriate for enhancing vaccination acceptance and uptake, and why.

Various reviews have focused on the demand-side of childhood vaccination (see Table 1 for a summary of these reviews). Many of these reviews are out of date, limited in geographical scope (i.e. include studies only from HICs), focused on specific vaccines or broader populations than children, and are not 'systematic' in their approach. In addition, few existing reviews include qualitative studies, and amongst those that do, in most cases the results were synthesised quantitatively or in a narrative summary.

Carrying out an up-to-date qualitative review that systematically explores the factors influencing vaccination acceptance from the perspective of parents and informal caregivers, across a variety of regions and vaccines, will provide a single point of access for synthesised qualitative evidence on vaccination acceptance to inform immunisation decision-making and strategies.

How this synthesis links to the intervention

The findings of this qualitative evidence synthesis will complement those of a Cochrane qualitative evidence synthesis on perceptions and experiences of communication about routine childhood vaccination (Ames 2017). As the review authors explain, communication is one of many interacting factors that may influence parents' and informal caregivers' decisions to take their children for vaccination, and communication alone will therefore not address all aspects of vaccine acceptance, hesitancy or refusal. Our review will therefore build upon this review by identifying the range of factors (in addition to vaccination communication and information) that may influence vaccination acceptance, and by explaining how these factors potentially operate to impact on vaccination acceptance.

This qualitative evidence synthesis will supplement existing Cochrane Reviews on the effectiveness of different interventions for improving childhood vaccination coverage and uptake (Saeterdal 2014; Oyo-Ita 2016; Jacobson 2018; Kaufman 2018). It may provide partial explanations for the heterogeneity of results across these Cochrane Reviews, as well as contributing to the development of more relevant, acceptable and effective interventions in the future. The results from this synthesis may help to improve our understanding of the reasons for acceptance of childhood vaccination from the perspective of parents and informal caregivers, and can be used to generate hypotheses about why and how certain interventions to improve vaccine uptake might be more effective than others, for whom, and in which contexts, for subsequent subgroup analyses in future effectiveness reviews. Finally, this review will provide insights from qualitative review data, which could be used in the development or refinement of conceptual models explaining parental vaccination acceptance, so that these models are informed by a larger evidence base and are potentially more theoretically grounded.

OBJECTIVES

1. Identify, appraise and synthesise qualitative studies exploring: parents' and informal caregivers' views, experiences, or decision-making regarding routine childhood vaccination; or the factors influencing acceptance of routine childhood vaccination arising from parents' and informal caregivers' accounts.

2. Develop a conceptual understanding of what and how different factors influence parental acceptance of routine childhood vaccination.

3. Explore how the findings of this review can enhance our understanding of the related intervention reviews (Saeterdal 2014; Oyo-Ita 2016; Jacobson 2018; Kaufman 2018).

METHODS

Review author reflexivity

At the outset of this review, all the review authors believed that childhood vaccination is a valuable individual and public health intervention, but that complex barriers exist to successful vaccination acceptance and uptake. Our review team comprises authors with varying disciplinary backgrounds: sociology (SC), anthropology (BS, AS, CC), psychology (CB, NL, SC), health systems (NL), vaccinology (CW), and epidemiology (BS, ES, CC, CW). We anticipate that having a multidisciplinary team, with varying perspectives from different authors, will facilitate our analysis and help identify and explain the multiple potential factors influencing vaccination acceptance. However, we will as a team remain mindful of our presuppositions and support each other to minimise the risk of different viewpoints skewing our analysis or the interpretation of our findings. Many of the review authors have considerable prior knowledge of existing conceptual frameworks on vaccine acceptance, and one author (CB) helped develop the extended 'C framework' (Betsch 2015; Betsch 2018). These factors may influence our analysis and interpretation of evidence. Progress and preliminary findings will be discussed regularly among the team, with the aim of identifying assumptions in the data synthesis, clarifying procedures and documenting various challenges faced in the review process. We will also use refutational analysis techniques ('disconfirming analyses'), such as exploring and explaining contradictory findings between studies, to further enhance the reflexive stance of the review team. We will account for these differences, and any other issues that may contribute to the interpretation of the review findings, by describing them in the 'Reflexivity' section of the full review.

Criteria for considering studies for this synthesis

Types of studies

We will include primary studies that use qualitative study designs such as ethnography, phenomenology, case studies, grounded theory studies and qualitative process evaluations. We will include studies that use both qualitative methods for data collection (e.g.

focus group discussions, individual interviews, observation, diaries, document analysis, and open-ended survey questions) and qualitative methods for data analysis (e.g. thematic analysis, framework analysis, grounded theory). We will exclude studies that collect data using qualitative methods but do not analyse these data using qualitative analysis methods (e.g. open-ended survey questions where the response data are analysed using descriptive statistics only). We will include mixed methods studies where it is possible to extract the data that were collected and analysed using qualitative methods. We will include studies regardless of whether or not they are linked to an intervention. We will not exclude any studies based on our assessment of methodological limitations, but will utilise this information to assess our confidence in the synthesis findings.

Topic of interest

The topic of interest in this synthesis is the factors which influence the acceptance of routine childhood vaccination from the perspective of parents and informal caregivers.

Types of participants

The review will include studies that report on views, experiences, decision-making or factors influencing acceptance regarding routine childhood vaccination, as given by parents or informal caregivers. By 'informal caregiver' we mean anyone who is directly involved in caring for the child or making the decision to vaccinate the child, or who has the responsibility to take the child for vaccination (Ames 2017). We will include studies if they report on the views, experiences, decision-making or acceptance of routine childhood vaccination, as given by prospective parents (e.g. pregnant women, their partners, or both). We will exclude papers if they only report what healthcare providers, policy-makers, programme administrators and managers or other immunisation stakeholders' say about the views, experiences or decision-making of parents and informal caregivers or the factors influencing vaccination acceptance.

Types of interventions

We will include studies about parents' or informal caregivers' views, experiences, decision-making or acceptance regarding routine childhood vaccination irrespective of the vaccination setting or mode of delivery. Vaccination settings and modes of delivery may include, for example, vaccination provided at healthcare facilities or fixed outreach sites, or by mobile health teams in communities (Machingaidze 2013b).

By 'routine' childhood vaccination we mean WHO-recommended routine vaccines for children under six years of age as part of the Expanded Programme on Immunization (EPI). This will include the following vaccines or combinations of vaccines (WHO 2018b).

1. Bacillus Calmette-Guérin (BCG)
2. Hepatitis B
3. Polio
    i) Oral poliovirus vaccine (OPV)
    ii) Inactivated polio vaccine (IPV)
4. Diphtheria, tetanus, and pertussis-containing
5. *Haemophilus influenzae* type b (Hib)
6. Pneumococcal conjugate vaccines (PCV)
7. Rotavirus
8. Measles
9. Mumps
10. Rubella
11. Measles, mumps and rubella (MMR)
12. Japanese encephalitis
13. Yellow fever
14. Tick-borne encephalitis
15. Typhoid
16. Cholera
17. Meningococcal
18. Hepatitis A
19. Seasonal influenza

We will not include the following vaccines because children under six years of age do not routinely receive them as part of the EPI.

1. Human papillomavirus (HPV)
2. Rabies
3. Haemagglutinin type 1 and neuraminidase type 1 (H1N1), and other epidemic vaccinations.

We will exclude studies on hypothetical vaccines, future vaccines or vaccination trials. We will also exclude studies if it is not possible to separate out the data on views of routine childhood vaccination from views of vaccination in other age groups (e.g. adolescents, adults) or views on vaccination in general.

Setting

We will include studies from any setting globally where childhood vaccination is provided. These settings could include healthcare facilities, fixed outreach sites and mobile health teams in communities.

Search methods for identification of studies

Electronic searches

We will search PDQ-Evidence (pdq-evidence.org) for related reviews in order to identify eligible studies for inclusion. We will also search the following electronic databases to identify eligible studies.

1. MEDLINE (Ovid)
2. Embase (Ovid)
3. CINAHL (EBSCO)
4. Anthropology Plus (EBSCO)

5. Web of Science Core Collection (Clarivate Analytics)
6. PsycINFO (Ovid)

Using guidelines developed by the Cochrane Qualitative & Implementation Methods Group for searching for qualitative evidence (Harris 2018), we will develop search strategies for each database. We will not apply any limits on language or geographic location. We will search all databases from 1974 to the date of search. This date range is intended to capture parents' and informal caregivers' views and experiences of routine childhood vaccination since the introduction of the WHO's EPI. We will include a methodological filter for qualitative studies. See Appendix 1 for the MEDLINE search strategy, which we will adapt for other databases. We will provide appendices detailing all strategies used.

Searching other resources

We will review the reference lists of all the included studies and key references (i.e. relevant systematic reviews). We will also conduct a cited reference search for all included studies on Web of Science and Google Scholar to determine whether they were cited by other relevant papers.

Data collection, management and synthesis

Selection of studies

We will collate records identified from different sources into one database and remove duplicates. Two review authors (SC, ES) will use Covidence (https://www.covidence.org) to independently assess the titles and abstracts of the identified records to evaluate eligibility. We will retrieve the full text of all the papers identified as potentially relevant by one or both review authors. These papers will then be assessed independently by the same two review authors (SC, ES). Disagreements will be resolved via discussion or, when required, by seeking a third review author's opinion. Where appropriate, we will contact the study authors for further information. We will include a table listing the studies excluded from our synthesis at the full-text stage, and the main reasons for exclusion. Where the same study (using the same sample and methods) has been presented in different reports, we will collate these reports so that each study (rather than each report) is the unit of interest in the review. We will include a PRISMA flow diagram to show our search results and the process of screening and selecting studies for inclusion.

Translation of languages other than English

Articles will only be selected if they are published in languages spoken by the review authors. We have chosen this approach due to the challenges associated with translating papers reporting qualitative research, the resources required for this, and our use of a meta-ethnographic approach which requires a full understanding of the meaning of concepts. This means that articles in French, English and German will be included. For papers published in French or German, we will attempt to translate the core meaning of the relevant themes or concepts into English. However, we acknowledge that some phrases and concepts are difficult to translate from one language into another, and that what constitutes the most appropriate translation is a judgement.

Sampling of studies

Large numbers of studies can impair the quality of the analysis in qualitative evidence syntheses (Ames 2017). Moreover, syntheses of qualitative studies aim for greater variation in concepts and depth of understanding, as opposed to an exhaustive overview of every study (Hannes 2013). Therefore, once all eligible studies have been identified, we will consider whether the amount of data in the included studies is too large and could impact the quality of the synthesis. If this is the case, we will sample from the included studies. Here we will explore the appropriateness of different purposeful sampling strategies (Suri 2011). One option might be to deploy a maximum variation (heterogeneity) sampling approach. This will comprise identifying potential areas of variation (e.g. geographic setting, type of health settings, type of vaccine, country income level, and study method), creating a sampling frame based on these dimensions and then mapping all eligible studies onto the frame (Suri 2011). A second option might be to use a theoretical sampling approach, whereby specific constructs and associated operational definitions will be predetermined, and studies will be selected based on their revelation of important theoretical insights about the predetermined constructs (Suri 2011). We will make decisions about whether to deploy sampling, and if so which strategy to use, once all eligible studies have been identified and we are more familiar with the available literature.

Data extraction

We will perform data extraction using a data extraction form designed specifically for this review. The form will be used to extract information on: first study author, date of publication, country of study, context (urban, rural; high-income country, low- and middle-income country), participant groups (first-time parent/informal caregiver, older parent/informal caregiver, etc.), number of participants, vaccine, study design, objectives, guiding theoretical or conceptual framework, and data collection and analysis methods.

Data management and synthesis

We will use a meta-ethnographic approach, following the steps outlined originally by Noblit and Hare (Noblit 1988), and the eMERGe meta-ethnography reporting guidance (France 2019).

Meta-ethnography is an interpretive, rather than aggregative, qualitative synthesis approach which is well-suited to producing new concepts, theories and theoretical models (France 2014; Noyes 2018). As a central aim of this synthesis is to derive new conceptual understandings of the factors influencing parents' and informal caregivers' acceptance of routine childhood vaccination, we decided that a meta-ethnographic approach was the most appropriate synthesis method. Meta-ethnography involves induction and interpretation to translate and synthesise conceptual data identified within included studies into a higher-order interpretation. The analysis is built up study by study, in a manner that both preserves the context of the primary data within individual studies, and facilitates an understanding of how concepts in different studies are related to each other (France 2019).

We will begin by identifying conceptual data (e.g. concepts, themes, ideas, metaphors) through reading and rereading the included studies. In this process, participant quotes will be understood as reflecting primary themes or first-order constructs. Secondary themes or second-order constructs will be understood as concepts developed by the authors of primary studies (Britten 2002). However, we recognise that all constructs are the result of author selection and interpretation (Schutz 1971). One review author (SC) will extract first- and second-order constructs, as well as relevant data on study characteristics and contexts, from all the studies. Two other authors (BS, NL) will extract these data from a sample of studies. Data will be extracted from the full primary studies and any additional linked online files of papers where available. The three authors (SC, BS, NL) will compare their extractions and resolve any differences through discussion and reference to the original studies.

The findings, as well as other potential aspects of the studies (such as research design, contextual factors), will then be compared to determine how studies are related. A wide variety of methods exist for this process; we will make a decision about the most appropriate method for comparison once we are more familiar with the included studies. One author (SC) will lead the process of comparison, with discussion and input from the rest of the review team.

The next step will involve translating the studies into each other. We will consider doing a 'reciprocal analysis' to translate concepts from individual studies into one another, or a 'refutational analysis' to explain differences and to explore and explain incongruities, exceptions and inconsistencies. We will make a decision regarding which translational approach to use (or a combination of both) once we have determined whether the studies and concepts within the studies relate reciprocally or refutationally (or both). Three review authors (SC, BS, NL) will conduct the translation, returning to the full text of papers frequently to ensure the emerging translation is meaningful.

The final step will involve a 'lines of argument synthesis' to develop synthesised translations (or third-order interpretations) and an overarching conceptual framework. We will compare the translated themes and interpretations, considering if and how they might be linked. Three review authors (SC, BS, NL) will consider the linkages and develop an initial conceptual framework which describes the factors influencing parental acceptance of childhood vaccination. At this stage, we will examine other, existing frameworks on vaccination acceptance (See 'Description of the topic' section, above). We will consider whether our initial framework 'fits' with any existing framework(s); whether our initial framework can be used to refine/adapt/amend any existing framework(s); or whether our initial framework suggests a new conceptual framework needs to be developed. These considerations will be discussed between the three authors (SC, BS, NL), and then the rest of the review team, to develop an integrated, refined or new conceptual framework. The conceptual framework will be discussed and reworked until a team consensus is reached. This final framework will provide a theoretical understanding of what, and how, different factors come together to influence parental acceptance of childhood vaccination. It will resemble a re-interpretation of meaning across studies, and represent more than an aggregative descriptive account (Barnett-Page 2009). This framework will also potentially be used to link our findings with the related Cochrane intervention reviews (Saeterdal 2014; Oyo-Ita 2016; Jacobson 2018; Kaufman 2018).

Assessment of methodological limitations in the included studies

Our inclusion criteria specify that included studies need to use both qualitative data collection and analysis methods. This constitutes a basic quality threshold as we will exclude studies that have used qualitative methods to collect data but not to analyse these data. In addition, two review authors (SC, BS) will independently assess methodological limitations for each study using an adaptation of the Critical Appraisal Skills Programme (CASP) quality assessment tool for qualitative studies (Atkins 2008; CASP 2013). Disagreements will be resolved through discussion between the two authors or through consultation with a third author (AS or CC). The adapted tool includes the following 8 questions which will be used to assess methodological limitations.

1. Are the setting(s) and context described adequately?
2. Is the sampling strategy described, and is this appropriate?
3. Is the data collection strategy described and justified?
4. Is the data analysis described, and is this appropriate?
5. Are the claims made/findings supported by sufficient evidence?
6. Is there evidence of reflexivity?
7. Does the study demonstrate sensitivity to ethical concerns?
8. Any other concerns?

We will conduct a pilot on three included studies to assess the feasibility of the use of this tool and ensure integrity of the assessment. We will not use the quality assessment approach to exclude studies but rather to judge the relative contribution of each study to the development of explanations and relationships and as part

of the assessment of how much confidence we have in each finding (see below). We will report our assessment of methodological limitations for each study in the 'Characteristics of included studies' tables.

Assessment of confidence in the synthesis findings

Two review authors (SC, BS) will use the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research) approach to summarise our confidence in each finding (Lewin 2018). CERQual assesses confidence in the evidence, based on the following four key components.

1. Methodological limitations of included studies: the extent to which there are concerns about the design or conduct of the primary studies that contributed evidence to an individual review finding.
2. Coherence of the review finding: an assessment of how clear and cogent the fit is between the data from the primary studies and a review finding that synthesises those data. By cogent, we mean well supported or compelling.
3. Adequacy of the data contributing to a review finding: an overall determination of the degree of richness and quantity of data supporting a review finding.
4. Relevance of the included studies to the review question: the extent to which the body of evidence from the primary studies supporting a review finding is applicable to the context (perspective or population, phenomenon of interest, setting) specified in the review question.

After assessing each of the four components, we will make a judgement about the overall confidence in the evidence supporting the review finding. We will judge confidence as high, moderate, low, or very low. The final assessment will be based on consensus among the review authors. All findings start as high confidence and will then be graded down if there are important concerns regarding any of the CERQual components.

'Summary of Qualitative Findings' table

To facilitate understanding and use of the review findings, we will present them in a 'Summary of Qualitative Findings' (SoQF) table. The table will display a structured summary of each review finding and references to the studies contributing data to each finding. It will also provide our assessment of confidence in the evidence as well as an explanation of this assessment, based on the GRADE-CERQual approach (Lewin 2018). All review findings will be reported in the SoQF table regardless of their associated level of confidence. The final conceptual framework developed will also be presented in a summarised narrative, and visually if appropriate.

Linking the synthesised qualitative findings to a Cochrane intervention review

As part of data synthesis, we plan to explore how the findings from our review relate to the findings of the related Cochrane intervention reviews (Saeterdal 2014; Oyo-Ita 2016; Jacobson 2018; Kaufman 2018). Our review findings might help to explain and contextualise why some interventions to improve vaccination uptake are effective (or more effective) and some are not, and may help generate hypotheses about potential important differences (e.g. setting, population, or vaccine) for planned subgroup analyses in future effectiveness reviews. Our review may also help identify factors that are considered important to parents and informal caregivers, for consideration in future intervention development and trials. The findings of this review will also complement those from a Cochrane qualitative evidence synthesis on parents' and informal caregivers' views and experiences of communication about routine childhood vaccination (Ames 2017).

We will explore the appropriateness of using two different supplementation approaches, and make a decision based on our synthesis findings. One option will be to deploy a logic model approach (Glenton 2013; Shepherd 2014), to link the review findings with a selection of conclusions and outcomes drawn by the intervention reviews. This will involve using the conceptual framework developed through our review as a starting point to develop a logical flow of theoretical hypotheses through which different factors, based on evidence from the qualitative synthesis, could affect the outcomes explored in the related Cochrane intervention reviews. The objective will be to present theories or assumptions about possible links, rather than to 'prove' causal associations. A second option will be to use a matrix model approach (Thomas 2004; Candy 2011), to configure and compare the findings of the reviews. This will involve developing a comparative table to explore how the reviews relate, and how the findings from the qualitative review inform the findings from the intervention reviews and vice-versa. For example, we might consider whether the interventions studied in the related Cochrane reviews contain or address features that parents and informal caregivers identified as important, or perceived as facilitators to vaccination acceptance. At least two review authors will work together to assess how our findings relate to the results of the intervention reviews, and how best to present them.

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* *Indicates the major publication for the study*

ADDITIONAL TABLES

Table 1. Summary of related published reviews focused on the demand-side of childhood vaccination (beliefs, attitudes, perceptions, decision-making, acceptance, hesitancy, confidence/trust)

Author/ date	Title	Focus	Methodology
Mills 2005	Systematic review of qualitative studies exploring parental beliefs and attitudes toward childhood vaccination identifies common barriers to vaccination	Focuses on parental beliefs and attitudes toward childhood vaccination and associated barriers to paediatric immunisations. Only includes studies from HICs	Qualitative
Karafillakis 2017	The benefit of the doubt or doubts over benefits? A systematic literature review of perceived risks of vaccines in European populations	Focuses on perceptions of the benefits and risks of vaccines. Only includes studies from Europe and considers vaccines for all age groups	Mixed methods, includes both quantitative and qualitative studies
Carlsen 2016	The swine flu vaccine, public attitudes, and researcher interpretations: a systematic review of qualitative research	Focuses on attitudes towards a vaccine given in response to a pandemic and also considers all age groups	Qualitative
Yaqub 2014	Attitudes to vaccination: a critical review	Focuses on vaccination attitudes among the public and healthcare professionals. Only includes studies from Europe and considers vaccines for all age groups	Mixed methods, includes both quantitative and qualitative studies
Sturm 2005	Parental beliefs and decision making about child and adolescent immunization: from polio to sexually transmitted infections	A narrative review focusing on the influence of parental attitudes and beliefs on vaccine decision-making Only includes studies from HICs and considers vaccines for children and adolescents	Mixed methods, includes both quantitative and qualitative studies
Brown 2010	Factors underlying parental decisions about combination childhood vaccinations including MMR: a systematic review	Focuses on the factors influencing vaccination decisions. Only includes studies from HICs and considers only combination MMR vaccines	Mixed methods, includes both quantitative and qualitative studies
Corben 2016	To close the childhood immunization gap, we need a richer understanding of parents' decision-making	A narrative review focusing on factors influencing parents' vaccination decision-making and interventions to increase vaccination uptake	Mixed methods, includes both quantitative and qualitative studies
Dube 2018	Underlying factors impacting vaccine hesitancy in high income countries: a review of qualitative studies	Focuses on the determinants of parents' attitudes and behaviors towards childhood vaccination. Only includes studies from HICs	Qualitative

Table 1. Summary of related published reviews focused on the demand-side of childhood vaccination (beliefs, attitudes, perceptions, decision-making, acceptance, hesitancy, confidence/trust) (*Continued*)

Jackson 2008	A systematic review of decision support needs of parents making child health decisions	Focuses on all parental decision-making about child health, not just vaccination	Mixed methods, includes both quantitative and qualitative studies
Ames 2017	Parents' and informal caregivers' views and experiences of communication about routine childhood vaccination: a synthesis of qualitative evidence	Focuses specifically on views and experiences of communication interventions about childhood vaccinations	Qualitative
Roberts 2002	Factors affecting uptake of childhood immunisation: a Bayesian synthesis of qualitative and quantitative evidence	Focuses on the factors that affect the uptake of recommended childhood immunisations. Only includes studies from HICs	Mixed
Nagaraj 2006	Does qualitative synthesis of anecdotal evidence with that from scientific research help in understanding public health issues: a review of low MMR uptake	Focuses on professional and parental factors underlying uptake of MMR only and only includes studies from HICs	Qualitative, includes technical and non-technical anecdotal literature
Rainey 2011	Reasons related to non-vaccination and under-vaccination of children in LMICs: Findings from a systematic review of the published literature, 1999-2009	Focuses on the factors related to the under-vaccination and non-vaccination of children. Considers both demand- and supply- related factors and only includes studies from LMICs	Mixed methods, includes both quantitative and qualitative studies
Favin 2012	Why children are not vaccinated: a review of the grey literature	A review of grey literature focusing on the reasons for childhood incomplete or non-vaccination. Considers both demand- and supply-related factors	Mixed methods, includes both quantitative and qualitative studies
Tauil 2016	Factors associated with incomplete or delayed vaccination across countries: A systematic review	Focuses on the factors influencing adherence to routine childhood immunisation schedule. Considers both demand- and supply-related factors	Quantitative
Falagas 2008	Factors associated with suboptimal compliance to vaccinations in children in developed countries: a systematic review	Focuses on the factors associated with suboptimal childhood vaccination compliance. Only includes studies from HICs	Quantitative
Dube 2013	Vaccine hesitancy: an overview	A narrative review providing an overview of the phenomenon of vaccine hesitancy and the possible causes of its increase, and the	Unclear as it includes multiple studies and reviews and does not specify the methods for each

Table 1. Summary of related published reviews focused on the demand-side of childhood vaccination (beliefs, attitudes, perceptions, decision-making, acceptance, hesitancy, confidence/trust) (*Continued*)

		determinants of individual vaccination decision-making. Only includes studies from HICs	
Larson 2014	Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: a systematic review of published literature, 2007-2012	Focuses on the factors affecting vaccine hesitancy and its determinants	Quantitative
Williams 2014	What are the factors that contribute to parental vaccine-hesitancy and what can we do about it?	Focuses on the barriers to vaccination reported by vaccine-hesitant parents and the current evidence on strategies to address parental vaccine hesitancy. Considers vaccines for both children and adolescents	Quantitative
Larson 2018b	Measuring trust in vaccination: a systematic review	Focuses specifically on the issue of trust and how different dimensions of trust interact to influence vaccine acceptance, hesitancy and refusal. Considers vaccines for both children and adolescents.	Mixed methods, includes both quantitative and qualitative studies

LMICs: low- and middle-income countries; **HICs:** high-income countries; **MMR:** measles, mumps and rubella

APPENDICES

Appendix 1. MEDLINE search strategy

#	Searches	Results
1	Vaccination Refusal/ or Anti Vaccination Movement/	152
2	Vaccination/ or Mass Vaccination/ or Immunization/ or Immunization Programs/	129219
3	"Patient Acceptance of Health Care"/ or Refusal to Participate/ or Treatment Refusal/ or Health knowledge, attitudes, practice/	144823

(*Continued*)

4	2 and 3	4053
5	((vaccin* or immunis* or immuniz*) and (attitude* or prespective* or perception* or belief* or concern* or view or views or accept* or hesita* or refus* or reject* or abstain* or declin* or resist* or object* or deny* or denier* or decision*)).ti	5326
6	((vaccin* or immunis* or immuniz*) adj2 (attitude* or prespective* or perception* or belief* or concern* or view or views or accept* or hesita* or refus* or reject* or abstain* or declin* or resist* or object* or deny* or denier* or decision*)).ab	5985
7	((vaccin* or immunis* or immuniz*) adj2 (attitude* or prespective* or perception* or belief* or concern* or view or views or accept* or hesita* or refus* or reject* or abstain* or declin* or resist* or object* or deny* or denier* or decision*)).kf	357
8	(anti vaccin* or antivaccin*).ti,ab,kf.	528
9	((vaccination or immunisation or immunization) adj (behavior or behaviour)).ti,ab,kf	188
10	or/5-9	10182
11	exp Vaccines/ or Vaccination/ or Mass Vaccination/ or Vaccination Coverage/ or Immunization/ or Immunization Programs/	274293
12	(vaccin* or immunis* or immuniz*).ti,ab,kf.	362639
13	11 or 12	429576
14	exp Child/	1795009
15	(child* or infant* or newborn* or new born* or neonat* or baby or babies or toddler*).ti,ab,kf	1823880
16	14 or 15	2716547
17	Parents/ or Parental Consent/ or Parenting/ or Mothers/ or Fathers/	108867
18	(parent* or mother* or father* or informal caregiver*).ti,ab,kf	562255
19	17 or 18	586757
20	13 and 16 and 19	12136
21	4 or 10 or 20	22238

(*Continued*)

22	limit 21 to "qualitative (maximizes specificity)"	800
23	21 and (Qualitative Research/ or Interviews as Topic/)	641
24	21 and (qualitative or group discussion? or focus group? or themes).ti,ab,kf	1005
25	or/22-24	1324
26	1 or 25	1469
27	("1974" or "1975" or "1976" or "1977" or "1978" or "1979" or "1980" or "1981" or "1982" or "1983" or "1984" or "1985" or "1986" or "1987" or "1988" or "1989" or "1990" or "1991" or "1992" or "1993" or "1994" or "1995" or "1996" or "1997" or "1998" or "1999" or "2000" or "2001" or "2002" or "2003" or "2004" or "2005" or "2006" or "2007" or "2008" or "2009" or "2010" or "2011" or "2012" or "2013" or "2014" or "2015" or "2016" or "2017" or "2018").yr	24895452
28	26 and 27	1469

CONTRIBUTIONS OF AUTHORS

Sara Cooper and Charles Wiysonge conceived the topic and Sara Cooper wrote the first draft. All review authors made substantial intellectual input to the protocol and approved the final version for submission.

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Sara Cooper: none known.

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